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NEWS  6  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
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NEWS  9  Jun 03  New e-mail delivery for search results now available
NEWS 10  Jun 10  MEDLINE Reload
NEWS 11  Jun 10  PCTFULL has been reloaded
NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                 saved answer sets no longer valid
NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
NEWS 15  Jul 30  NETFIRST to be removed from STN
NEWS 16  Aug 08  CANCERLIT reload
NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18  Aug 08  NTIS has been reloaded and enhanced
NEWS 19  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                 now available on STN
NEWS 20  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22  Aug 26  Sequence searching in REGISTRY enhanced
NEWS 23  Sep 03  JAPIO has been reloaded and enhanced
NEWS 24  Sep 16  Experimental properties added to the REGISTRY file
NEWS 25  Sep 16  Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26  Sep 16  CA Section Thesaurus available in CAPLUS and CA

NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
              CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
              AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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FILE 'EMBASE' ENTERED AT 18:04:57 ON 24 SEP 2002

FILE 'BIOSIS' ENTERED AT 18:04:57 ON 24 SEP 2002

FILE 'SCISEARCH' ENTERED AT 18:04:57 ON 24 SEP 2002

FILE 'CAPLUS' ENTERED AT 18:04:57 ON 24 SEP 2002

=> s modified allergen
L1 283 MODIFIED ALLERGEN

=> s l1 and IgE epitope
L2 1 L1 AND IGE EPITOPE

=> d l2 cbib abs

L2 ANSWER 1 OF 1 SCISEARCH COPYRIGHT 2002 ISI (R)
1999:544997 The Genuine Article (R) Number: 214EK. Genetically engineered plant allergens with reduced anaphylactic activity. Singh M B (Reprint); deWeerd N; Bhalla P L. UNIV MELBOURNE, INST LAND & FOOD RESOURCES, PLANT MOL BIOL & BIOTECHNOL LAB, PARKVILLE, VIC 3052, AUSTRALIA (Reprint). INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY (JUN 1999) Vol. 119, No. 2, pp. 75-85. Publisher: KARGER. ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND. ISSN: 1018-2438. Pub. country: AUSTRALIA. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Allergy immunotherapy is based on the administration of increasing amounts of the disease-eliciting allergens in order to yield allergen-specific non-responsiveness. Success of this therapy is associated with modulation of the immune response to allergenic molecules at the level of T-helper cells and the induction of blocking antibodies. The extracts used for immunotherapy are highly heterogenous preparations from natural sources and contain additional components, mostly proteins which are not well defined, Recombinant DNA technology offers novel tools for production of pure and well-characterised allergens for specific immunotherapy. However, high IgE reactivity of pure recombinant allergens is associated with an increased risk of potentially life-threatening anaphylactic reactions. A major improvement in allergen-specific immunotherapy may be achieved by using genetically engineered recombinant allergens with reduced anaphylactic activity. Recently the site-directed mutagenesis technique has been applied successfully to produce variants of major grass, birch and oilseed rape allergens with reduced IgE reactivity but retained T-cell reactivity. These **modified allergens** with reduced anaphylactic potential are novel candidates for safer and more effective allergen-specific immunotherapy.

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=> dup remove l1
PROCESSING COMPLETED FOR L1
L3          157 DUP REMOVE L1 (126 DUPLICATES REMOVED)

=> s l3 and foold
L4            0 L3 AND FOOLD

=> s l3 and food allergen
L5            2 L3 AND FOOD ALLERGEN

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PROCESSING COMPLETED FOR L2
L6            1 DUP REMOVE L2 (0 DUPLICATES REMOVED)

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L6   ANSWER 1 OF 1  SCISEARCH  COPYRIGHT 2002 ISI (R)
1999:544997   The Genuine Article (R) Number: 214EK. Genetically engineered
     plant allergens with reduced anaphylactic activity.  Singh M B (Reprint);
     deWeerd N; Bhalla P L. UNIV MELBOURNE, INST LAND & FOOD RESOURCES, PLANT
     MOL BIOL & BIOTECHNOL LAB, PARKVILLE, VIC 3052, AUSTRALIA (Reprint).
     INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY (JUN 1999) Vol. 119, No.
     2, pp. 75-85. Publisher: KARGER. ALLSCHWILERSTRASSE 10, CH-4009 BASEL,
     SWITZERLAND. ISSN: 1018-2438. Pub. country: AUSTRALIA. Language: English.
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB       Allergy immunotherapy is based on the administration of increasing
     amounts of the disease-eliciting allergens in order to yield
     allergen-specific non-responsiveness. Success of this therapy is
     associated with modulation of the immune response to allergenic molecules
     at the level of T-helper cells and the induction of blocking antibodies.
     The extracts used for immunotherapy are highly heterogenous preparations
     from natural sources and contain additional components, mostly proteins
     which are not well defined, Recombinant DNA technology offers novel tools
     for production of pure and well-characterised allergens for specific
     immunotherapy. However, high IgE reactivity of pure recombinant allergens
     is associated with an increased risk of potentially life-threatening
     anaphylactic reactions. A major improvement in allergen-specific
     immunotherapy may be achieved by using genetically engineered recombinant
     allergens with reduced anaphylactic activity. Recently the site-directed
     mutagenesis technique has been applied successfully to produce variants of
     major grass, birch and oilseed rape allergens with reduced IgE reactivity
     but retained T-cell reactivity. These modified allergens
     with reduced anaphylactic potential are novel candidates for safer and
     more effective allergen-specific immunotherapy.


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     (FILE 'HOME' ENTERED AT 18:04:46 ON 24 SEP 2002)

     FILE 'EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 18:04:57 ON 24 SEP
     2002
L1          283 S MODIFIED ALLERGEN
L2            1 S L1 AND IGE EPITOPE
L3          157 DUP REMOVE L1 (126 DUPLICATES REMOVED)
L4            0 S L3 AND FOOLD
L5            2 S L3 AND FOOD ALLERGEN
L6            1 DUP REMOVE L2 (0 DUPLICATES REMOVED)

=> s l3 and substitution
L7            3 L3 AND SUBSTITUTION

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L8 3 DUP REMOVE L7 (0 DUPLICATES REMOVED)

=> d l8 1-3 cbib abs

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.

AB It has been detd. that allergens, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by masking the site with a compd. that prevents IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the IgE-binding epitope, to eliminate IgE binding. The method allows the protein to be altered as minimally as possible, other than within the IgE-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut allergens to demonstrate alteration of IgE binding sites. The crit. amino acids within each of the IgE binding epitopes of the peanut protein that are important to Ig binding have been detd. **Substitution** of even a single amino acid within each of the epitopes led to loss of IgE binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to IgE binding.

L8 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1991:313676 Document No.: BA92:24191. STANDARDIZATION OF GLUTARALDEHYDE-MODIFIED TYROSINE-ADSORBED ALLERGEN EXTRACTS. OVERELL B G; SPACKMAN D A; WHEELER A W; PFEIFER P. STRESEMANNALLEE 6, W-4040 NEUSS 1.. ALLERGOLOGIE, (1991) 14 (3), 110-115. CODEN: ALLRDI. ISSN: 0344-5062. Language: German.

AB A new assessment of the allergoid properties of glutaraldehyde-modified grass pollen extract has been made in order to validate standardization procedures. Increasing **substitution** of amino groups with glutaraldehyde led to a loss of allergenicity of extracts, as measured by RAST inhibition and by histamine release from sensitized human basophils. Both modified and unmodified materials induced IgG antibody in guinea-pigs. The antibody-stimulating capacity of the modified matrials could not be accounted for by the presence of unmodified activity in the modified samples. The antibodies induced by modified materials had a spectrum of specificities similar to that induced by unmodified extract, these specificities appearing to be directed at allergenic components when assessed by SDS-PAGE immunoblotting. One such specificity was to a major allergen component R7 (Lol p I) of temperate grass pollen. Since immunoreactivity with rabbit IgG antibody specific for R7 was retained in all the modified samples, a basis for an assay for standardization of glutaraldehyde-**modified allergen** products was established. The rationale for the use of this assay, and its use in establishing "standardized unit" system is explained.

L8 ANSWER 3 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
81023748 EMBASE Document No.: 1981023748. Suppression of reaginic antibodies with **modified allergens**. III. Preparation of tolerogenic conjugates of common allergens with monomethoxypolyethylene glycols of different molecular weights by the mixed anhydride method. Wie S.I.; Wie C.W.; Lee W.Y.; et al.. Dept. Immunol., Univ. Manitoba Bas. Med. Sci. Bldg., Winnipeg, Manitoba R3E 0W3, Canada. International Archives of Allergy and Applied Immunology 64/1 (84-99) 1981.
CODEN: IAAAAM. Pub. Country: Switzerland. Language: English.
AB Our previous findings that antigens, such as ovalbumin (OA) and the extract of ragweed pollen (RAG), could be rendered nonantigenic, nonallergenic and tolerogenic by conjugation with polyethylene glycol (PEG) have been extended in the present to the synthesis of conjugates of a variety of antigens with monofunctional monomethoxy-PEGs (mPEGs) of different molecular weights by the use of the mixed anhydride method. Thus, mPEGs with molecular weights of 2,000, 5,000, 10,000 and 20,000 were coupled to proteins such as dog serum albumin (DA), bovine pancreatic ribonuclease, OA and the constituents of pollen, helminth and bacterial allergens (RAG, Timothy grass pollen, Ascaris suum and Micropolyspora faeni). All these mPEG conjugates depressed markedly the ongoing IgE antibody formation in sensitized animals, in spite of additional injections of the sensitizing dose of the appropriate antigen. Moreover, the allergenicity of the proteins was either totally abolished or markedly reduced after coupling to mPEGs. Conjugates of DA and OA of varying degree of **substitution** (i.e. number of mPEG molecules attached per protein molecule) were prepared with mPEGs of different molecular weights and their immunological properties were assessed. It appears that, for a series of tolerogenic conjugates of the same antigen, there exists some inverse relationship between the degree of **substitution** and the molecular weight of mPEG, i.e. a high level of tolerogenicity with a concomitant reduction or total loss of allergenicity was achieved with a lower degree of **substitution** utilizing mPEGs of increasing molecular weights. On the basis of these results, it is concluded that a variety of allergens may be converted by conjugation with mPEGs to tolerogenic products with a potential for use in the therapy of patients allergic to a wide spectrum of common allergens.

=> s l3 and reduce IgE binding
L9 0 L3 AND REDUCE IGE BINDING

=> s l3 and IgE binding
L10 15 L3 AND IGE BINDING

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L11 15 DUP REMOVE L10 (0 DUPLICATES REMOVED)

=> d l11 1-15 cbib abs

L11 ANSWER 1 OF 15 SCISEARCH COPYRIGHT 2002 ISI (R)
2002:530650 The Genuine Article (R) Number: 563MD. Modification of peanut allergen Ara h 3: Effects on **IgE binding** and T cell stimulation. Rabjohn P; West C M; Connaughton C; Sampson H A; Helm R M (Reprint); Burks A W; Bannon G A. Univ Arkansas Med Sci, ACHRI, Dept Biochem & Mol Biol, Slot 512, 1120 Marshall St, Little Rock, AR 72202 USA (Reprint); Univ Arkansas Med Sci, ACHRI, Dept Biochem & Mol Biol, Little Rock, AR 72202 USA; Univ Arkansas Med Sci, ACHRI, Dept Pediat, Little Rock, AR 72202 USA; Mt Sinai Sch Med, Dept Pediat, New York, NY USA. INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY (MAY 2002) Vol. 128, No. 1, pp. 15-23. Publisher: KARGER. ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND. ISSN: 1018-2438. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background: Peanut allergy is a major health concern due to the increased prevalence, potential severity, and chronicity of the reaction. The cDNA encoding a third peanut allergen, Ara h 3, has been previously cloned and characterized. Mutational analysis of the Ara h 3 **IgE -binding** epitopes with synthetic peptides revealed that single amino acid changes at critical residues could diminish **IgE binding**. Methods: Specific oligonucleotides were used in polymerase chain reactions to modify the cDNA encoding Ara h 3 at critical **IgE binding** sites. Four point mutations were introduced into the Ara h 3 cDNA at codons encoding critical amino acids in epitopes 1, 2, 3 and 4. Recombinant modified proteins were used in SDS-PAGE/Western IgE immunoblot, SDS-PAGE/Western IgE immunoblot inhibition and T cell proliferation assays to determine the effects of these changes on in vitro clinical indicators of peanut hypersensitivity. Results: Higher amounts of modified Ara h 3 were required to compete with the wild-type allergen for peanut-specific serum IgE. Immunoblot analysis with individual serum IgE from Ara-h-3-allergic patients showed that **IgE binding** to the modified protein decreased similar to35-85% in comparison to **IgE binding** to wildtype Ara h 3. Also, the modified Ara h 3 retained the ability to stimulate T cell activation in PBMCs donated by Ara-h-3-allergic patients. Conclusions: The engineered hypoallergenic Ara h 3 variant displays two characteristics essential for recombinant allergen immunotherapy; it has a reduced binding capacity for serum IgE from peanut-hypersensitive patients and it can stimulate T-cell proliferation and activation. Copyright (C) 2002 S, Karger AG, Basel.

L11 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2002 ACS
2001:608578 Document No. 136:84234 Hunting the magic bullet in immunotherapy: New forms of old treatment or something completely different?. Fearby, S.; Frew, A. J. (University Department of Medical Specialities, Southampton General Hospital, Southampton, SO16 6YD, UK). Clinical and Experimental Allergy, 31(7), 969-974 (English) 2001. CODEN: CLEAEN. ISSN: 0954-7894. Publisher: Blackwell Science Ltd..
AB A review discussing immunotherapy for allergic diseases using recombinant allergens, chem. **modified allergens** (allergoids), adjuvants, and peptides and **IgE-binding** haptens.

L11 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS
2002:212344 Document No. 137:108505 Comparison of allergens in genetically modified soybean with conventional soybean. Park, Jae Hyun; Chung, Seung Tae; Kim, Jae Hee; Kim, Ji Young; Noh, Geun Woong; Kim, Dong Sup; Kim, Hyung Soo (Department of Toxicology, National Institute of Toxicological Research, Korea Food and Drug Administration, Seoul, 122-704, S. Korea). Yakhak Hoechi, 45(3), 293-301 (Korean) 2001. CODEN: YAHOA3. ISSN: 0513-4234. Publisher: Pharmaceutical Society of Korea.
AB The objective of this research was to compare the allergens of genetically modified (GM) soybean (Roundup Ready) with conventional soybean. Soybean exts. were prepd. as crude exts., heated exts., and heated and simulated gastric fluid (SGF)-digested samples to characterize the stability of allergens to physicochem. treatment. Pos. sera from 20 soybean-sensitive patients and control sera from 5 normal subjects were used to identify the endogenous allergens in soybean. Specific-**IgE binding** activities to each soybean prepn. were evaluated by ELISA and immunoblot technique. In ELISA results, **IgE binding** activities of pos. sera to soy crude exts. generally showed two fold higher mean value than those of control sera, however there was no significant difference between GM soybean and natural soybean varieties. Extd. proteins from each soybean prepn. were sepd. with SDS-PAGE. The band pattern of GM soybean was very similar to those of natural soybean varieties. Immunoblots for the different soybeans revealed no differences in **IgE-binding** protein patterns, moreover, disclosed five prominent **IgE-binding** bands (75, 70, 50, 44 and 34 kDa) in crude exts., four (75, 70, 44 and 34 kDa) in heated prepn., one

(50 kDa) in heated and SGF-digested prepns. These **IgE binding** bands were consistent with previously reported results on soybean. The obtained results indicate that GM soybean (Roundup Ready) is no different from natural soybean in terms of its allergen.

L11 ANSWER 4 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2001145729 EMBASE Engineering, characterization and in vitro efficacy of the major peanut allergens for use in immunotherapy. Bannon G.A.; Cockrell G.; Connaughton C.; West C.M.; Helm R.; Stanley J.S.; King N.; Rabjohn P.; Sampson H.A.; Burks A.W.. Dr. G.A. Bannon, UAMS, 4301 W. Markham, Little Rock, AR 72205, United States. bannongarya@exchange.uams.edu. International Archives of Allergy and Immunology 124/1-3 (70-72) 2001. Refs: 12.
ISSN: 1018-2438. CODEN: IAAIEG. Pub. Country: Switzerland. Language: English. Summary Language: English.
AB Background: Numerous strategies have been proposed for the treatment of peanut allergies, but despite the steady advancement in our understanding of atopic immune responses and the increasing number of deaths each year from peanut anaphylaxis, there is still no safe, effective, specific therapy for the peanut-sensitive individual. Immunotherapy would be safer and more effective if the allergens could be altered to reduce their ability to initiate an allergic reaction without altering their ability to desensitize the allergic patient. Methods: The cDNA clones for three major peanut allergens, Ara h 1, Ara h 2, and Ara h 3, have been cloned and characterized. The **IgE-binding** epitopes of each of these allergens have been determined and amino acids critical to each epitope identified. Site-directed mutagenesis of the allergen cDNA clones, followed by recombinant production of the **modified allergen**, provided the reagents necessary to test our hypothesis that hypoallergenic proteins are effective immunotherapeutic reagents for treating peanut-sensitive patients. Modified peanut allergens were subjected to immunoblot analysis using peanut-positive patient sera IgE, T cell proliferation assays, and tested in a murine model of peanut anaphylaxis. Results: In general, the **modified allergens** were poor competitors for binding of peanut-specific IgE when compared to their wild-type counterpart. The **modified allergens** demonstrated a greatly reduced **IgE-binding** capacity when individual patient serum IgE was compared to the binding capacity of the wild-type allergens. In addition, while there was considerable variability between patients, the **modified allergens** retained the ability to stimulate T cell proliferation. Conclusions: These **modified allergen** genes and proteins should provide a safe immunotherapeutic agent for the treatment of peanut allergy. Copyright .COPYRGT. 2001 S. Karger AG, Basel.

L11 ANSWER 5 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000295013 EMBASE T cell reactivity with allergoids: Influence of the type of APC. Kahlert H.; Grage-Griebenow E.; Stuwe H.-T.; Cromwell O.; Fiebig H.. Dr. H. Kahlert, Allergopharma, Joachim Ganzer KG, Hermann-Korner-Strasse 52, D-21465 Reinbek, Germany. allergopharmakg@csi.com. Journal of Immunology 165/4 (1807-1815) 15 Aug 2000.
Refs: 65.
ISSN: 0022-1767. CODEN: JOIMA3. Pub. Country: United States. Language: English. Summary Language: English.
AB The use of allergoids for allergen-specific immunotherapy has been established for many years. The characteristic features of these chemically **modified allergens** are their strongly reduced **IgE binding** activity compared with the native form and the retained immunogenicity. T cell reactivity of chemically **modified allergens** is documented in animals, but in humans indirect evidence of reactivity has been concluded from the induction of allergen-specific IgG during immunotherapy. Direct evidence of T cell reactivity was obtained recently using isolated human T cells.

To obtain further insight into the mechanism of action of allergoids, we compared the Ag-presenting capacity of different APC types, including DC and macrophages, generated from CD14+ precursor cells from the blood of grass pollen allergic subjects, autologous PBMC, and B cells. These APC were used in experiments together with Phl p 5-specific T cell clones under stimulation with grass pollen allergen extract, rPhl p 5b, and the respective allergoids. Using DC and macrophages, allergoids exhibited a pronounced and reproducible T cell- stimulating capacity. Responses were superior to those with PBMC, and isolated B cells failed to present allergoids. Considerable IL-12 production was observed only when using the DC for Ag presentation of both allergens and allergoids. The amount of IL-10 in supernatants was dependent on the phenotype of the respective T cell clone. High IL-10 production was associated with suppressed IL-12 production from the DC in most cases. In conclusion, the reactivity of Th cells with allergoids is dependent on the type of the APC.

L11 ANSWER 6 OF 15 SCISEARCH COPYRIGHT 2002 ISI (R)
2000:404901 The Genuine Article (R) Number: 317QM. Mechanisms of allergen-specific immunotherapy. Akdis C A; Blaser K (Reprint). SWISS INST ALLERGY & ASTHMA RES, OBERE STR 22, CH-7270 DAVOS, SWITZERLAND (Reprint); SWISS INST ALLERGY & ASTHMA RES, CH-7270 DAVOS, SWITZERLAND. ALLERGY (JUN 2000) Vol. 55, No. 6, pp. 522-530. Publisher: MUNKSGAARD INT PUBL LTD. 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK. ISSN: 0105-4538. Pub. country: SWITZERLAND. Language: English.

L11 ANSWER 7 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000152493 EMBASE Modulation of allergen-specific immune responses to the major shrimp allergen, tropomyosin, by specific targeting to scavenger receptors on macrophages. Rajagopal D.; Ganesh K.A.; Subba Rao P.V.. Prof. P.V. Subba Rao, Vittal Mallaya Scientific Res. Fndn., KR Road, Bangalore 560004, India. pvs@vmsrf.com. International Archives of Allergy and Immunology 121/4 (308-316) 2000.
Refs: 51.
ISSN: 1018-2438. CODEN: IAAIEG. Pub. Country: Switzerland. Language: English. Summary Language: English.

AB Background: Tropomyosin from shrimp is the major cross-reacting crustacean food allergen. Earlier studies have led to the purification and immunochemical characterization of the major **IgE binding** epitopes of the allergen. Maleylated proteins are known to be specifically targeted to scavenger receptors on macrophage. Since antigens processed and presented by macrophages are known to elicit Th1 type of responses and allergic responses are characterized by polarization towards Th2 phenotype, the possibility of modulation of allergen-specific immune responses by targeting of tropomyosin to macrophage via scavenger receptor was explored. Methods: The IgG and **IgE binding** potential of the native maleylated form of tropomyosin was carried out by ELISA and immunoblot. The ability of the native and maleylated form of allergen to induce in vitro proliferation of splenocytes from BALB/C mice immunized with both forms of allergen was tested. The in vitro production of IL-4 and IFN-.gamma. by splenocytes from mice immunized with the two forms of allergen was determined from culture supernatants. The in vivo production of serum IgG1 and IgG2a antibodies following immunization with native and **modified allergens** was monitored by ELISA.
Results: The maleylated form of tropomyosin was found to have reduced antigenicity and allergenicity as compared to its native counterpart. The **modified allergen** was, however, found to elicit a cellular response similar to native tropomyosin in vitro. Analysis of the cytokine profiles showed a modulation from an IL-4-dominant, proallergic, Th2 phenotype to an IFN-.gamma.-dominant, antiallergic, Th1 phenotype that could also be correlated to a modulation in the in vivo antibody isotype.
Conclusion: The results suggest the possible potential for modulating allergic responses in vivo by selective targeting to macrophages.

L11 ANSWER 8 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000152488 EMBASE Regulation of specific immune responses by chemical and structural modifications of allergens. Akdis C.A.; Blaser K.. Dr. C.A. Akdis, SIAF, Obere Strasse 22, CH-7270 Davos, Switzerland. akdisac@siaf.unizh.ch. International Archives of Allergy and Immunology 121/4 (261-269) 2000.
Refs: 103.
ISSN: 1018-2438. CODEN: IAAIEG. Pub. Country: Switzerland. Language: English. Summary Language: English.
AB Specific immunotherapy (SIT) is an efficient treatment of allergic diseases to defined allergens. Despite being used in clinical practice since early in this century, more rational and safer regimens are required, because SIT is faced with the risk of anaphylaxis and standardization problems of allergen-extract-based treatments. A better understanding of the pathogenesis of allergy and of the mechanisms of SIT has led to various approaches to overcome these problems. Knowledge of the influence of IgE-facilitated antigen presentation on allergen-specific Th2 responses increased the efforts to generate non-**IgE-binding** allergens. The current principal approach to allergen modification is to modify B cell epitopes in order to prevent **IgE binding** and effector cell cross-linking while preserving T cell epitopes to retain the capacity of inducing tolerance. In this way, the **modified allergen** will be directed to T cells by a phagocytosis/ pinocytosis-mediated antigen uptake mechanism, by-passing IgE cross-linking and IgE-dependentantigen presentation. Accordingly, a differential regulation of allergen-specific T cell cytokine patterns and IgE:IgG production was demonstrated by modifications of the three-dimensional structure of allergens because of linearity in T cell epitopes and conformation dependence in B cell epitopes. In this context, chemically **modified allergen** extracts with low **IgE-binding** capacity have been developed to reduce anaphylactic side effects since the early 1980s. The progress of recombinant techniques for producing allergens and allergen derivatives has led to a dramatic improvement in the ability of developing novel vaccines for the treatment of allergy. This has enabled mutation or deletion of decisive amino acids in B cell epitopes and fractionation or oligomerization of allergens by genetic engineering as fruitful approaches to generate hypoallergenic vaccines. Moreover, non-**IgE-binding** short T cell epitope peptides and single-amino-acid-altered peptide ligands represent potential candidates for future SIT. Copyright (C) 2000 S. Karger AG, Basel.

L11 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2002 ACS
1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.
AB It has been detd. that allergens, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be modified to be less allergenic by modifying the **IgE binding** sites. The **IgE binding** sites can be converted to non-**IgE binding** sites by masking the site with a compd. that prevents

IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the **IgE-binding** epitope, to eliminate **IgE binding**. The method allows the protein to be altered as minimally as possible, other than within the **IgE-binding** sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut allergens to demonstrate alteration of **IgE binding** sites. The crit. amino acids within each of the **IgE binding** epitopes of the peanut protein that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of **IgE binding**. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to **IgE binding**.

L11 ANSWER 10 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

97237173 EMBASE Document No.: 1997237173. Preseasonal specific immunotherapy with modified Phleum pratense allergenic extracts: Tolerability and effects. Ricca V.; Ciprandi G.; Pesce G.; Riccio A.; Varese P.; Pecora S.; Canonica G.W.. S. Pecora, Neo Abello, Via Falzarego, 8, 20021 Ospiate di Bollate, Milano, Italy. Allergologia et Immunopathologia 25/4 (167-175) 1997.

Refs: 34.

ISSN: 0301-0546. CODEN: AGIMBJ. Pub. Country: Spain. Language: English. Summary Language: English; Spanish.

AB The preparation of chemically **modified allergens**, with a reduced **IgE binding** capacity (responsible for side effects with traditional immunotherapy) but with the same or greater immunogenic activity, is one of the paths followed to obtain better results with specific immunotherapy (IT). The aim of the study was to evaluate the tolerability and effects of an extract Phleum pratense, modified with glutaraldehyde and absorbed on aluminium hydroxide, in controlling the seasonal symptomatology induced by grass pollen in a group of 10 monosensitized patients, compared to a group of 10 similar patients not treated with specific IT but with drugs alone. The monitoring parameters were: 1) Clinical: a) symptomatology after specific conjunctival provocation test (pre and post seasonal) and during the natural exposure to the allergen b) drug consumption. 2) Immunological (peripheral blood eosinophils, total and specific IgE, total specific IgG). 3) Cytological, before, during and after the pollen season. Conclusions: In subjects treated with specific IT a) both the overall symptomatology and the drug consumption resulted significantly reduced compared to the controls ($p = 0.045$); b) the phlogistic infiltrate showed a tendency to decrease during the pollen season; c) the peripheral blood eosinophils, total and specific IgE and IgG did not show any significant variation compared to the controls; d) no systemic reactions occurred and there were only two slight local reactions.

L11 ANSWER 11 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

97010841 EMBASE Document No.: 1997010841. Preseasonal specific immunotherapy with modified Phleum pratense allergenic extracts: Tolerability and effects. Vittorio R.; Giorgio C.; Giampaola P.; Annamaria R.; Paola V.; Silvia P.; Giorgio Walter C.. R. Vittorio, Servizio di Allergologia, Ospedale Koelliker dei Missionari, Maria S.S. Consolata, Torino, Italy. Allergologia et Immunopathologia 24/6 (255-262) 1996.

Refs: 34.

ISSN: 0301-0546. CODEN: AGIMBJ. Pub. Country: Spain. Language: English. Summary Language: English; Italian.

AB The preparation of chemically **modified allergens**, with a reduced **IgE binding** capacity (responsible for side effects with traditional immunotherapy) but with the same or greater

immunogenic activity, is one of the paths followed to obtain better results with specific immunotherapy (IT). The aim of the study was to evaluate the tolerability and effects of extracts of Phleum pratense, modified with glutaraldehyde and absorbed on aluminium hydroxide, in controlling the seasonal symptomatology induced by grass pollen in a group of 10 monosensitized patients, compared to a group of 10 similar patients not treated with specific IT but with drugs alone. The monitoring parameters were: 1) Clinical: a) symptomatology after specific conjunctival provocation test (pre and post seasonal) and during the natural exposure to the allergen b) drug consumption. 2) Immunological (peripheral blood eosinophils, total and specific IgE, total specific IgG). 3) Cytological, before, during and after the pollen season. Conclusions: In subjects treated with specific IT a) both the overall symptomatology and the drug consumption resulted significantly reduced compared to the controls ($p = 0.045$); b) the phlogistic infiltrate showed a tendency to decrease during the pollen season; c) the peripheral blood eosinophils, total and specific IgE and IgG did not show any significant variation compared to the controls; d) no systemic reactions occurred and there were only two slight local reactions.

L11 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS
1995:680795 Document No. 123:81614 Recombinant preparation of **modified allergen** Der fII as antiallergic agents.
Nishama, Chiharu; Juki, Toshifumi; Okumura, Yasushi; Shibuya, Ichiro (Asahi Breweries Ltd, Japan; Torii Yakuhin Kk; Nikka Whisky). Jpn. Kokai Tokkyo Koho JP 07095887 A2 19950411 Heisei, 50 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1993-275897 19930929.
AB Allergen Der fII of Dermatophagoides farinae is modified by replacing certain residues with Ala to lower its **IgE-binding** activities. The **modified allergen** can be produced by expressing its coding gene in an eukaryotic host and used as an antiallergic agent.

L11 ANSWER 13 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
94305698 EMBASE Document No.: 1994305698. [Clinical and experimental trends in hyposensitization]. KLINISCHE UND EXPERIMENTELLE TRENDS DER HYPOSENSIBILISIERUNG. Jager L.. Humboldtstrasse 3,D-07740 Jena, Germany. Allergologie 17/9 (400-403) 1994.
ISSN: 0344-5062. CODEN: ALLRDI. Pub. Country: Germany. Language: German. Summary Language: German; English.
AB Hyposensitization has been developed starting from a wrong idea. Only during the last 15 years methods for an exact analysis of the underlying mechanisms became available - especially due to the progress in immunology. The first step was the characterization and purification of allergens from natural sources. The next one was the identification of **IgE-binding** epitopes. At present research activities are concentrated on T cell epitopes. By their means, above all, a modulation of the immune response could be achieved. This will be the scientifically-based way to the development of **modified allergen**.

L11 ANSWER 14 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
94225059 EMBASE Document No.: 1994225059. Modified par j I allergen from P. judaica pollen and its rate of absorption in rats. Mistrello G.; Roncarolo D.; Gentili M.; Zanoni D.; Falagiani P.. Research Department, Laboratorio Farmaceutico Lofarma, Viale Cassala 40,20143 Milano, Italy. Immunology Letters 40/1 (31-36) 1994.
ISSN: 0165-2478. CODEN: IMLED6. Pub. Country: Netherlands. Language: English. Summary Language: English.
AB Polymerized allergens (allergoids) have been introduced in the immunotherapy of allergic disease in order to reduce the risk of side effects. However, their high molecular weight can be a limit, particularly when they are administered by a route involving passage through the

mucosal barrier. We describe a simple procedure aimed at developing an original **modified allergen** with significantly less allergenic potential (intended as human **IgE-binding** capacity) but preserving the monomeric nature of the molecule. Par j I, the major allergen of Parietaria judaica pollen, was purified by a combination of monoclonal antibodies and affinity chromatography. Par j I allergen was then modified by reaction with potassium cyanate (KCNO), and compared with the native allergen to evaluate its allergenic potency (RAST-inhibition) and molecular weight-(SDS-PAGE). **Modified allergen** showed significantly lower allergenic potency but kept its original molecular weight, making it particularly suitable for buccal (sublingual) administration. To study the adsorption profile, modified Par j I was radiolabeled and administered intravenously and sublingually to normal rats. The prospects for clinical application of the **modified allergen** are discussed.

L11 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2002 ACS
1994:432588 Document No. 121:32588 Mapping of allergen epitopes by antibodies. Aalberse, R. C. (Cent. Lab. the Neth. Red Cross Blood Transfus. Serv., Amsterdam, 1066, Neth.). Adv. Allergol. Clin. Immunol., Proc. Eur. Congr., 15th, 103-7. Editor(s): Godard, Philippe; Bousquet, Jean; Michel, Francois-Bernard. Parthenon Publ. Group: Carnforth, UK. (English) 1992. CODEN: 59YQAO.
AB A review with 3 refs. discussing the specificity of IgE antibodies, why epitope mapping is of interest, procedures for mapping **IgE-binding** epitopes on allergens, inhibition by monoclonal anti-allergen antibodies, phylogenetic allergen variants, chem. or enzymically **modified allergens**, variant allergens prepd. by rDNA technol., and synthetic peptides.

=> l11 and legumes
L11 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l11 and legumes
L12 0 L11 AND LEGUMES

=> s l11 and fish
L13 1 L11 AND FISH

=> d l13 cbib abs

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.
AB It has been detd. that allergens, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be modified to be less allergenic by modifying the **IgE binding** sites. The

IgE binding sites can be converted to non-**IgE** **binding** sites by masking the site with a compd. that prevents **IgE binding** or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the **IgE-binding** epitope, to eliminate **IgE binding**. The method allows the protein to be altered as minimally as possible, other than within the **IgE-binding** sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut allergens to demonstrate alteration of **IgE binding** sites. The crit. amino acids within each of the **IgE binding** epitopes of the peanut protein that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of **IgE binding**. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to **IgE binding**.

```
=> s l11 and crustaceans
L14           0 L11 AND CRUSTACEANS

=> s l3 and shrimp
L15           1 L3 AND SHRIMP

=> d l15 cbib as
'AS' IS NOT A VALID FORMAT FOR FILE 'EMBASE'

The following are valid formats:

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ABS --------- AB
ALL --------- AN, DN, TI, AU, CS, SO, PUI, CY, DT, FS, LA, SL, AB,
              CT, RN, CN, NP, CO, GEN
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CBIB -------- Compressed bibliographic data
DALL -------- ALL, delimited for post-processing
IABS -------- ABS, with a text label
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
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TRIAL ------  TI, CT, RN, CN, NP, CO, GEN
 (SAM, TRI)
HIT --------- All fields containing hit terms
HITIND ------ IND
KWIC -------- All hit terms plus 20 words on either side
OCC --------- List of display fields containing hit terms
              and number of occurrences in each field

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To display a particular field or fields,  enter the display field
codes.  For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>).  Examples of formats include: 'BIB';
'AB'; 'SO,ST'.  You may specify the format fields in any order,
and the information will be displayed in the same order as the
format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be
used with the DISPLAY ACC command to display the record for a
specified Accession Number.
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ENTER DISPLAY FORMAT (BIB):abs

L15 ANSWER 1 OF 1 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AB Background: Tropomyosin from **shrimp** is the major cross-reacting crustacean food allergen. Earlier studies have led to the purification and immunochemical characterization of the major IgE binding epitopes of the allergen. Maleylated proteins are known to be specifically targeted to scavenger receptors on macrophage. Since antigens processed and presented by macrophages are known to elicit Th1 type of responses and allergic responses are characterized by polarization towards Th2 phenotype, the possibility of modulation of allergen-specific immune responses by targeting of tropomyosin to macrophage via scavenger receptor was explored. Methods: The IgG and IgE binding potential of the native maleylated form of tropomyosin was carried out by ELISA and immunoblot. The ability of the native and maleylated form of allergen to induce in vitro proliferation of splenocytes from BALB/C mice immunized with both forms of allergen was tested. The in vitro production of IL-4 and IFN-.gamma. by splenocytes from mice immunized with the two forms of allergen was determined from culture supernatants. The in vivo production of serum IgG1 and IgG2a antibodies following immunization with native and **modified allergens** was monitored by ELISA. Results: The maleylated form of tropomyosin was found to have reduced antigenicity and allergenicity as compared to its native counterpart. The **modified allergen** was, however, found to elicit a cellular response similar to native tropomyosin in vitro. Analysis of the cytokine profiles showed a modulation from an IL-4-dominant, proallergic, Th2 phenotype to an IFN-.gamma.-dominant, antiallergic, Th1 phenotype that could also be correlated to a modulation in the in vivo antibody isotype. Conclusion: The results suggest the possible potential for modulating allergic responses in vivo by selective targeting to macrophages. Copyright (C) 2000 S. Karger AG, Basel.

=> s l3 and eggs
L16 0 L3 AND EGGS

=> s l3 and egg
L17 4 L3 AND EGG

=> dup remove l17
PROCESSING COMPLETED FOR L17
L18 4 DUP REMOVE L17 (0 DUPLICATES REMOVED)

=> d l18 1-4 cbib abs

L18 ANSWER 1 OF 4 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2001120857 EMBASE [Peanut allergy]. ALLERGIE A L'ARACHIDE. Dutau G.; Rance F.. G. Dutau, Unite des maladies respiratoires, Hopital des Enfants, 330, avenue de Grande-Bretagne, 31026 Toulouse Cedex 3, France. Revue Francaise d'Allergologie et d'Immunologie Clinique 41/2 (187-198) 2001.
Refs: 98.
ISSN: 0335-7457. CODEN: RFAIBB. Pub. Country: France. Language: French. Summary Language: English; French.
AB Peanut allergy, which is frequent in the United States and was much less so in Europe up to the mid-eighties, has become a major problem in many industrialized countries. Peanut consumption is high in Eastern Europe, the United Kingdom, The Netherlands, Germany and France. The frequency of peanut allergy is between 0.5 and O.7% in the general population. Two million Americans are now thought to be affected. In France peanuts are one of the most frequent allergens, lying second (27.4 %) to **egg** in food allergies in children, and holding first place in food allergies in children aged over 3 years. Sensitization occurs through ingestion,

contact even if indirect, and inhalation. The symptoms, which affect the skin and the respiratory or gastrointestinal tract, appear a few minutes to a few hours after exposure. Serious reactions (anaphylactic shock, life-threatening reactions, sudden death) have been described. Asthma has a significantly higher association with peanut allergy than with other allergies, taken overall. As with other food allergies, diagnosis is based on history, prick-tests, screening for specific serum IgE and food challenge whose modalities (labial and oral challenge) are debated. For the time being, elimination is the only form of treatment. The development of a **modified allergen** as immunogenic as possible but practically without allergenic effects should give immunotherapy new impetus. Patients with severe peanut allergy should carry a card or wear a distinctive bracelet indicating their condition as well as an emergency kit including in particular epinephrine. .COPYRGT. 2001 Editions scientifiques et medicales Elsevier SAS.

L18 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS

1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.

AB It has been detd. that allergens, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by masking the site with a compd. that prevents IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the IgE-binding epitope, to eliminate IgE binding. The method allows the protein to be altered as minimally as possible, other than within the IgE-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut allergens to demonstrate alteration of IgE binding sites. The crit. amino acids within each of the IgE binding epitopes of the peanut protein that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of IgE binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to IgE binding.

L18 ANSWER 3 OF 4 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:170102 The Genuine Article (R) Number: YY214. Tolerogenic activity of polyethylene glycol-conjugated lysozyme distinct from that of the native counterpart. Ito H O (Reprint); So T; Hirata M; Koga T; Ueda T; Imoto T. KYUSHU UNIV, FAC DENT, DEPT BIOCHEM, FUKUOKA 81282, JAPAN (Reprint); KYUSHU UNIV, GRAD SCH PHARMACEUT SCI, FUKUOKA 81282, JAPAN. IMMUNOLOGY (FEB 1998) Vol. 93, No. 2, pp. 200-207. Publisher: BLACKWELL SCIENCE LTD. P O BOX 88, OSNEY MEAD, OXFORD, OXON, ENGLAND OX2 0NE. ISSN: 0019-2805. Pub. country: JAPAN. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Conjugation of proteins with polyethylene glycol (PEG) has been reported to make the proteins tolerogenic. Native proteins are also potentially tolerogenic when given without adjuvants. We compared

immunotolerogenic activities between PEG-conjugated and native hen **egg**-white lysozyme (HEL). BALB/c mice were given consecutive weekly intraperitoneal administrations of PEG-conjugated HEL, unmodified HEL or phosphate-buffered saline (PBS), for 3 weeks, then challenged with HEL in Freund's complete adjuvant. The pretreatment with PEG-HEL tolerized both T-cell and humoral responses, while native HEL tolerized only the T-cell response. Immunoglobulin G1 (IgG1) antibody was already elevated in HEL-pretreated mice prior to challenge immunization, followed by suppressed IgG2a and IgG2b. but spared IgG1 production after the antigen challenge. whereas PEG-HEL-pretreated mice produced no antibody in all IgG subclasses prior and subsequent to the antigen-challenge. Production of interleukin-2 (IL-2) and interferon-gamma (IFN-gamma) by lymphoid cells in response to HEL in vitro was markedly suppressed in both the antigen-pretreated groups. while suppression of IL-4 production was evident only in PEG-HEL-, not in HEL-pretreated animals. Involvement of suppressor cells in these tolerance states was found to be unlikely. and the immunological property of PEG-HEL differed from deaggregated HEL that was similar to the original HEL. These results suggest a unique immunotolerogenic activity of PEG-conjugated proteins to suppl css both T-helper type-1 (Th1)and Th2-type responses, the result bring extensive inhibition of all IgG subclass responses, while tolerance induction by unconjugated soluble proteins tends to be targeted on Th1-, but spares Th2-type responses.

L18 ANSWER 4 OF 4 SCISEARCH COPYRIGHT 2002 ISI (R)
96:271858 The Genuine Article (R) Number: UC578. REDUCED IMMUNOGENICITY OF MONOMETHOXYPOLYETHYLENE GLYCOL-MODIFIED LYSOZYME FOR ACTIVATION OF T-CELLS . SO T; ITO H O; KOGA T; UEDA T; IMOTO T (Reprint). KYUSHU UNIV, GRAD SCH PHARMACEUT SCI, FUKUOKA 81282, JAPAN (Reprint); KYUSHU UNIV, GRAD SCH PHARMACEUT SCI, FUKUOKA 81282, JAPAN; KYUSHU UNIV, SCH DENT, DEPT BIOCHEM, FUKUOKA 81282, JAPAN. IMMUNOLOGY LETTERS (JAN 1996) Vol. 49, No. 1-2, pp. 91-97. ISSN: 0165-2478. Pub. country: JAPAN. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Chemical modification of proteins with monomethoxypolyethylene glycol (mPEG) will reduce the immunogenicity of proteins. In the present study, we evaluated the effect of mPEG modification on the capacity of hen **egg**-white lysozyme (HEL) to stimulate T cells. Lymph node cells (LNCs) from mice immunized with HEL or with mPEG-HEL conjugate were cultured with these antigens, then we measured the proliferation and IL-2 production. mPEG-modification lowered the T cell-activating capacity of HEL, both in vitro and in vivo. Neither toxicity, nor antigen non-specific immunosuppressive capacity was observed with mPEG-HEL and unconjugated mPEG. Suppressor cells were unlikely to be generated in the mPEG-HEL-primed LNCs. We next examined the behavior of mPEG-HEL during antigen processing. The capacity of HEL and mPEG-HEL to be incorporated by live cells was much the same. However, the susceptibility to various proteases, including endosomal/lysosomal enzymes, was significantly decreased by mPEG modification. The increased resistance of mPEG-HEL to proteolytic degradation implied that the conjugate was poorly presented to T cells, This may be an important factor related to the low immunogenicity of mPEG modified proteins.

=> s l3 and hydrophilic amino acid substitution
L19 0 L3 AND HYDROPHILIC AMINO ACID SUBSTITUTION

=> d his

(FILE 'HOME' ENTERED AT 18:04:46 ON 24 SEP 2002)

FILE 'EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 18:04:57 ON 24 SEP 2002
L1 283 S MODIFIED ALLERGEN

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L2            1 S L1 AND IGE EPITOPE
L3          157 DUP REMOVE L1 (126 DUPLICATES REMOVED)
L4            0 S L3 AND FOOLD
L5            2 S L3 AND FOOD ALLERGEN
L6            1 DUP REMOVE L2 (0 DUPLICATES REMOVED)
L7            3 S L3 AND SUBSTITUTION
L8            3 DUP REMOVE L7 (0 DUPLICATES REMOVED)
L9            0 S L3 AND REDUCE IGE BINDING
L10          15 S L3 AND IGE BINDING
L11          15 DUP REMOVE L10 (0 DUPLICATES REMOVED)
L12           0 S L11 AND LEGUMES
L13           1 S L11 AND FISH
L14           0 S L11 AND CRUSTACEANS
L15           1 S L3 AND SHRIMP
L16           0 S L3 AND EGGS
L17           4 S L3 AND EGG
L18           4 DUP REMOVE L17 (0 DUPLICATES REMOVED)
L19           0 S L3 AND HYDROPHILIC AMINO ACID SUBSTITUTION

=> s l3 and IgE binding
L20          15 L3 AND IGE BINDING

=> s modified allergen
L21         283 MODIFIED ALLERGEN

=> s l21 and protein
L22          65 L21 AND PROTEIN

=> s l22 and IgE
L23          40 L22 AND IGE

=> dup remove l23
PROCESSING COMPLETED FOR L23
L24          23 DUP REMOVE L23 (17 DUPLICATES REMOVED)

=> d l24 1-23 cbib abs

L24  ANSWER 1 OF 23  SCISEARCH  COPYRIGHT 2002 ISI (R)
2002:530650   The Genuine Article (R) Number: 563MD. Modification of peanut
     allergen Ara h 3: Effects on IgE binding and T cell stimulation.
     Rabjohn P; West C M; Connaughton C; Sampson H A; Helm R M (Reprint); Burks
     A W; Bannon G A. Univ Arkansas Med Sci, ACHRI, Dept Biochem & Mol Biol,
     Slot 512, 1120 Marshall St, Little Rock, AR 72202 USA (Reprint); Univ
     Arkansas Med Sci, ACHRI, Dept Biochem & Mol Biol, Little Rock, AR 72202
     USA; Univ Arkansas Med Sci, ACHRI, Dept Pediat, Little Rock, AR 72202 USA;
     Mt Sinai Sch Med, Dept Pediat, New York, NY USA. INTERNATIONAL ARCHIVES OF
     ALLERGY AND IMMUNOLOGY (MAY 2002) Vol. 128, No. 1, pp. 15-23. Publisher:
     KARGER. ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND. ISSN: 1018-2438
     . Pub. country: USA. Language: English.
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB       Background: Peanut allergy is a major health concern due to the
     increased prevalence, potential severity, and chronicity of the reaction.
     The cDNA encoding a third peanut allergen, Ara h 3, has been previously
     cloned and characterized. Mutational analysis of the Ara h 3 IgE
     -binding epitopes with synthetic peptides revealed that single amino acid
     changes at critical residues could diminish IgE binding.
     Methods: Specific oligonucleotides were used in polymerase chain reactions
     to modify the cDNA encoding Ara h 3 at critical IgE binding
     sites. Four point mutations were introduced into the Ara h 3 cDNA at
     codons encoding critical amino acids in epitopes 1, 2, 3 and 4.
     Recombinant modified proteins were used in SDS-PAGE/Western
     IgE immunoblot, SDS-PAGE/Western IgE immunoblot
     inhibition and T cell proliferation assays to determine the effects of
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these changes on in vitro clinical indicators of peanut hypersensitivity. Results: Higher amounts of modified Ara h 3 were required to compete with the wild-type allergen for peanut-specific serum **IgE**. Immunoblot analysis with individual serum **IgE** from Ara-h-3-allergic patients showed that **IgE** binding to the modified **protein** decreased similar to35-85% in comparison to **IgE** binding to wildtype Ara h 3. Also, the modified Ara h 3 retained the ability to stimulate T cell activation in PBMCs donated by Ara-h-3-allergic patients. Conclusions: The engineered hypoallergenic Ara h 3 variant displays two characteristics essential for recombinant allergen immunotherapy; it has a reduced binding capacity for serum **IgE** from peanut-hypersensitive patients and it can stimulate T-cell proliferation and activation. Copyright (C) 2002 S, Karger AG, Basel.

L24 ANSWER 2 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 1
2001418237 EMBASE [Allergen immunotherapy - A position paper of the German society for allergology and clinical immunology]. DIE SPEZIFISCHE IMMUNTHERAPIE (HYPOSENSIBILISIERUNG) MIT ALLERGENEN: POSITIONSPAPIER DER DEUTSCHEN GESELLSCHAFT FUR ALLERGOLOGIE UND KLINISCHE IMMUNOLOGIE, INHALTLICH ABGESTIMMT MIT DEM ARZTEVERBAND DEUTSCHER ALLERGOLOGEN. Kleine-Tebbe J.; Fuchs Th.; Klimek L.; Kuhr J.; Lepp U.; Niggemann B.; Rakoski J.; Renz H.; Saloga J.; Simon J.. Dr. J. Kleine-Tebbe, Schlossstrasse 51, D-14059 Berlin, Germany. Allergologie 24/11 (535-544) 2001.
Refs: 37.
ISSN: 0344-5062. CODEN: ALLRDI. Pub. Country: Germany. Language: German. Summary Language: English; German.

AB Mechanisms of allergen immunotherapy (AIT) are complex, inducing numerous immunological effects. Successfull AIT is most likely based on a functional switch of and tolerance induction in specific T cells downregulating allergic hypersensitivity and inflammation. Subcutaneous AIT for allergic rhinoconjunctivitis and allergic asthma has been successfully assessed in controlled studies with several clinically important allergens (i.e. birch-, grass- and mugwortpollen, dust mites, animal dander) and has shown convincing clinical efficacy. Considered as the only causal treatment besides allergen avoidance at present, AIT can alter the natural course of allergic diseases. Hymenoptera venom hypersensitivity (to bee- and wasp venom) treated with AIT gives the best results compared to AIT with other allergens. AIT is indicated in patients with **IgE**-mediated sensitizations and corresponding clinical symptoms to allergens, which do not or hardly permit allergen avoidance and which are availabe as suitable extracts. Decisions about indication and allergen selection should only be made by a physician with certified training or qualified knowledge and skills in allergology. AIT is administered by physicians experienced in this therapy. After addressing tolerability and present status of health, the recommended or individually adjusted dose is injected and precisely documented, followed by a mandatory waiting period of 30 minutes. Indication for and application of AIT in children are quite similar compared to the treatment of adults. Children tolerate AIT very well and benefit especially from its immunomodulatory effects. Risk factors for and results of unwanted systemic effects can effectively be minimized by training of the staff members involved adhering to safety standards and immediate emergency treatment. **Modified allergens**, recombinant **proteins** and immunomodulatory adjuvants created by basic research are promises for an improved efficacy of AIT with reduced unwanted effects in the future.

L24 ANSWER 3 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2001340898 EMBASE [Allergen immunotheraphy - A position paper of the German society for allergology and clinical immunology]. DIE SPEZIFISCHE IMMUNTHERAPIE (HYPOSENSIBILISIERUNG) MIT ALLERGENEN: POSITIONSPAPIER DER DEUTSCHEN GESELLSCHAFT FUR ALLERGOLOGIE UND KLINISCHE IMMUNOLOGIE

INHALTLICH ABGESTIMMT MIT DEM ARZTEVERBAND DEUTSCHER ALLERGOLOGEN. Kleine-Tebbe J.; Fuchs T.; Klimek L.; Kuhr J.; Lepp U.; Niggemann B.; Rakoski J.; Renz H.; Saloga J.; Simon J.. Dr. J. Kleine-Tebbe, Schlossstr. 51, 14059 Berlin, Germany. kleine-tebbe@allergie-experten.de. Pneumologie 55/9 (438-444) 2001.
Refs: 37.
ISSN: 0934-8387. CODEN: PNEMEC. Pub. Country: Germany. Language: German. Summary Language: English; German.

AB Mechanisms of allergen immunotherapy (AIT) are complex inducing numerous immunological effects. Successful AIT is most likely based on a functional switch of and tolerance induction in specific T cells downregulating allergic hypersensitivity and inflammation. Subcutaneous AIT for allergic rhinoconjunctivitis and allergic asthma has been successfully assessed in controlled studies with several clinically important allergens (i.e. birch-, grass- and mugwortpollen, dust mites, animal dander) and has shown convincing clinical efficacy. Considered as the only causal treatment besides allergen avoidance at present, AIT can alter the natural course of allergic diseases. Hymenopteravenom hypersensitivity (to bee- and wasp venom) treated with AIT gives the best results compared to AIT with other allergens. AIT is indicated in patients with **IgE**-mediated sensitizations and corresponding clinical symptoms to allergens, which do not or hardly permit allergen avoidance and which are available as suitable extracts. Decisions about indication and allergen selection should only be made by a physician with certified training or qualified knowledge and skills in allergology. AIT is administered by physicians experienced in this therapy. After adressing tolerability and present status of health the recommended or individually adjusted does is injected and precisely documented, followed by a mandatory waiting period of 30 minutes. Indication for and application of AIT in children are quite similar compared to the treatment of adults. Children tolerate AIT very well and benefit especially from its immunomodulatory effects. Risk factors for and results of unwanted systemic effects can effectively be minimized by training of the staff members involved, adhering to safety standards and immediate emergency treatment. **Modified allergens**, recombinant **proteins** and immunomodulatory adjuvants created by basic research are promises for an improved efficacy of AIT with reduced unwanted effects in the future.

L24 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2002 ACS

2002:212344 Document No. 137:108505 Comparison of allergens in genetically modified soybean with conventional soybean. Park, Jae Hyun; Chung, Seung Tae; Kim, Jae Hee; Kim, Ji Young; Noh, Geun Woong; Kim, Dong Sup; Kim, Hyung Soo (Department of Toxicology, National Institute of Toxicological Research, Korea Food and Drug Administration, Seoul, 122-704, S. Korea). Yakhak Hoechi, 45(3), 293-301 (Korean) 2001. CODEN: YAHOA3. ISSN: 0513-4234. Publisher: Pharmaceutical Society of Korea.

AB The objective of this research was to compare the allergens of genetically modified (GM) soybean (Roundup Ready) with conventional soybean. Soybean exts. were prepd. as crude exts., heated exts., and heated and simulated gastric fluid (SGF)-digested samples to characterize the stability of allergens to physicochem. treatment. Pos. sera from 20 soybean-sensitive patients and control sera from 5 normal subjects were used to identify the endogenous allergens in soybean. Specific-**IgE** binding activities to each soybean prepn. were evaluated by ELISA and immunoblot technique. In ELISA results, **IgE** binding activities of pos. sera to soy crude exts. generally showed two fold higher mean value than those of control sera, however there was no significant difference between GM soybean and natural soybean varieties. Extd. **proteins** from each soybean prepn. were sepd. with SDS-PAGE. The band pattern of GM soybean was very similar to those of natural soybean varieties. Immunoblots for the different soybeans revealed no differences in **IgE**-binding **protein** patterns, moreover, disclosed five prominent **IgE**-binding bands (75, 70, 50, 44 and 34 kDa) in crude

exts., four (75, 70, 44 and 34 kDa) in heated prepn., one (50 kDa) in heated and SGF-digested prepns. These **IgE** binding bands were consistent with previously reported results on soybean. The obtained results indicate that GM soybean (Roundup Ready) is no different from natural soybean in terms of its allergen.

L24 ANSWER 5 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2
2001145729 EMBASE Engineering, characterization and in vitro efficacy of the major peanut allergens for use in immunotherapy. Bannon G.A.; Cockrell G.; Connaughton C.; West C.M.; Helm R.; Stanley J.S.; King N.; Rabjohn P.; Sampson H.A.; Burks A.W.. Dr. G.A. Bannon, UAMS, 4301 W. Markham, Little Rock, AR 72205, United States. bannongarya@exchange.uams.edu. International Archives of Allergy and Immunology 124/1-3 (70-72) 2001. Refs: 12.
ISSN: 1018-2438. CODEN: IAAIEG. Pub. Country: Switzerland. Language: English. Summary Language: English.

AB Background: Numerous strategies have been proposed for the treatment of peanut allergies, but despite the steady advancement in our understanding of atopic immune responses and the increasing number of deaths each year from peanut anaphylaxis, there is still no safe, effective, specific therapy for the peanut-sensitive individual. Immunotherapy would be safer and more effective if the allergens could be altered to reduce their ability to initiate an allergic reaction without altering their ability to desensitize the allergic patient. Methods: The cDNA clones for three major peanut allergens, Ara h 1, Ara h 2, and Ara h 3, have been cloned and characterized. The **IgE**-binding epitopes of each of these allergens have been determined and amino acids critical to each epitope identified. Site-directed mutagenesis of the allergen cDNA clones, followed by recombinant production of the **modified allergen**, provided the reagents necessary to test our hypothesis that hypoallergenic **proteins** are effective immunotherapeutic reagents for treating peanut-sensitive patients. Modified peanut allergens were subjected to immunoblot analysis using peanut-positive patient sera **IgE**, T cell proliferation assays, and tested in a murine model of peanut anaphylaxis. Results: In general, the **modified allergens** were poor competitors for binding of peanut-specific **IgE** when compared to their wild-type counterpart. The **modified allergens** demonstrated a greatly reduced **IgE**-binding capacity when individual patient serum **IgE** was compared to the binding capacity of the wild-type allergens. In addition, while there was considerable variability between patients, the **modified allergens** retained the ability to stimulate T cell proliferation. Conclusions: These **modified allergen** genes and **proteins** should provide a safe immunotherapeutic agent for the treatment of peanut allergy. Copyright .COPYRGT. 2001 S. Karger AG, Basel.

L24 ANSWER 6 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000330067 EMBASE [Allergen immunotherapy - A position paper of the German Society for Allergology and Clinical Immunology]. DIE SPEZIFISCHE IMMUNTHERAPIE (HYPOSENSIBILISIERUNG) MIT ALLERGENEN - POSITIONSPAPIER DER DEUTSCHEN GESELLSCHAFT FUR ALLERGOLOGIE UND KLINISCHE IMMUNOLOGIE. Kleine-Tebbe J.; Fuchs T.; Klimek L.; Kuhr J.; Lepp U.; Niggemann B.; Rakoski J.; Renz H.; Saloga J.; Simon J.. Dr. J. Kleine-Tebbe, Universitatshautklinik, Liebigstr. 21, 04103 Leipzig, Germany. Allergo Journal 9/6 (317-324) 2000.
Refs: 37.
ISSN: 0941-8849. CODEN: ALJOEY. Pub. Country: Germany. Language: German. Summary Language: English; German.

AB Mechanisms of allergen immunotherapy (AIT) are complex inducing numerous immunological effects. Successful AIT is most likely based on a functional switch of and tolerance induction in specific T cells downregulating allergic hypersensitivity and inflammation. Subcutaneous AIT for allergic

rhinoconjunctivitis and allergic asthma has been successfully assessed in controlled studies with several clinically important allergens (i.e. birch-, grass- and mugwortpollen, dust mites, animal dander) and has shown convincing clinical efficacy. Considered as the only causal treatment besides allergen avoidance at present, AIT can alter the natural course of allergic diseases. Hymenopteravenom hypersensitivity (to bee- and wasp venom) treated with AIT gives the best results compared to AIT with other allergens. AIT is indicated in patients with **IgE**-mediated sensitizations and corresponding clinical symptoms to allergens, which do not or hardly permit allergen avoidance and which are available as suitable extracts. Decisions about indication and allergen selection should only be made by a physician with certified training or qualified knowledge and skills in allergology. AIT is administered by physicians experienced in this therapy. After adressing tolerability and present status of health the recommended or individually adjusted dose is injected and precisely documented, followed by a mandatory waiting period of 30 minutes. Indication for and application of AIT in children are quite similar compared to the treatment of adults. Children tolerate AIT very well and benefit especially from its immunomodulatory effects. Risk factors for and results of unwanted systemic effects can effectively be minimized by training of the staff members involved, adhering to safety standards and immediate emergency treatment. **Modified allergens**, recombinant **proteins** and immunomodulatory adjuvants created by basic research are promises for an improved efficacy of AIT with reduced unwanted effects in the future.

L24 ANSWER 7 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 3
2000152493 EMBASE Modulation of allergen-specific immune responses to the major shrimp allergen, tropomyosin, by specific targeting to scavenger receptors on macrophages. Rajagopal D.; Ganesh K.A.; Subba Rao P.V.. Prof. P.V. Subba Rao, Vittal Mallaya Scientific Res. Fndn., KR Road, Bangalore 560004, India. pvs@vmsrf.com. International Archives of Allergy and Immunology 121/4 (308-316) 2000.
Refs: 51.
ISSN: 1018-2438. CODEN: IAAIEG. Pub. Country: Switzerland. Language: English. Summary Language: English.

AB Background: Tropomyosin from shrimp is the major cross-reacting crustacean food allergen. Earlier studies have led to the purification and immunochemical characterization of the major **IgE** binding epitopes of the allergen. Maleylated **proteins** are known to be specifically targeted to scavenger receptors on macrophage. Since antigens processed and presented by macrophages are known to elicit Th1 type of responses and allergic responses are characterized by polarization towards Th2 phenotype, the possibility of modulation of allergen-specific immune responses by targeting of tropomyosin to macrophage via scavenger receptor was explored. Methods: The IgG and **IgE** binding potential of the native maleylated form of tropomyosin was carried out by ELISA and immunoblot. The ability of the native and maleylated form of allergen to induce in vitro proliferation of splenocytes from BALB/C mice immunized with both forms of allergen was tested. The in vitro production of IL-4 and IFN-.gamma. by splenocytes from mice immunized with the two forms of allergen was determined from culture supernatants. The in vivo production of serum IgG1 and IgG2a antibodies following immunization with native and **modified allergens** was monitored by ELISA. Results: The maleylated form of tropomyosin was found to have reduced antigenicity and allergenicity as compared to its native counterpart. The **modified allergen** was, however, found to elicit a cellular response similar to native tropomyosin in vitro. Analysis of the cytokine profiles showed a modulation from an IL-4-dominant, proallergic, Th2 phenotype to an IFN-.gamma.-dominant, antiallergic, Th1 phenotype that could also be correlated to a modulation in the in vivo antibody isotype. Conclusion: The results suggest the possible potential for modulating allergic responses in vivo by selective targeting to macrophages. Copyright (C)

2000 S. Karger AG, Basel.

L24 ANSWER 8 OF 23 SCISEARCH COPYRIGHT 2002 ISI (R)
2000:98117 The Genuine Article (R) Number: 279EH. Reduced immunogenicity of beta-lactoglobulin by conjugation with carboxymethyl dextran. Hattori M (Reprint); Nagasawa K; Ohgata K; Sone N; Fukuda A; Matsuda H; Takahashi K. TOKYO UNIV AGR & TECHNOL, FAC AGR, DEPT APPL BIOL SCI, 3-5-8 SAIWAI CHO, FUCHU, TOKYO 1838509, JAPAN (Reprint); TOKYO UNIV AGR & TECHNOL, FAC AGR, DEPT VET CLIN, FUCHU, TOKYO 1838509, JAPAN. BIOCONJUGATE CHEMISTRY (JAN-FEB 2000) Vol. 11, No. 1, pp. 84-93. Publisher: AMER CHEMICAL SOC. 1155 16TH ST, NW, WASHINGTON, DC 20036. ISSN: 1043-1802. Pub. country: JAPAN. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We prepared two beta-lactoglobulin (beta-LG)-carboxymethyl dextran (CMD) conjugates (Conj. 10A and Conj. 10B) by using a water-soluble carbodiimide to decrease the immunogenicity of beta-LG, The molar ratios of beta-LG to CMD in the conjugates were 5:1 (Conj. 10A) and 2:1 (Conj. 10B). The beta-LG-CMD conjugates maintained the retinol-binding activity of native beta-LG. Intrinsic fluorescence study indicated that shielding of the surface of beta-LG by CMD occurred in each conjugate, which was eminent in Conj. 10B. A local conformational change around (125)Thr-(135)Lys (alpha-helix) in each conjugate was detected by ELISA with monoclonal antibodies. The denaturation temperature of beta-LG evaluated by differential scanning calorimetry was greatly enhanced in each conjugate. The anti-beta-LG antibody response was markedly reduced after immunization with the beta-LG-CMD conjugates in BALB/c, C57BL/6,and C3H/He mice. We determined the B cell epitopes of beta-LG and each conjugate recognized in these mice and found that the linear epitope profiles of the beta-LG-CMD conjugates were similar to those of beta-LG, while the antibody response for each epitope was dramatically reduced. The reduced immunogenicity of beta-LG was most marked in the case of Conj. 10B, which contained more CMD than Conj. 10A, and was effectively shielded by CMD. We concluded that masking of epitopes by CMD is responsible for the decreased immunogenicity of the beta-LG in these conjugates.

L24 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2002 ACS
1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.
AB It has been detd. that allergens, which are characterized by both humoral (**IgE**) and cellular (T cell) binding sites, can be modified to be less allergenic by modifying the **IgE** binding sites. The **IgE** binding sites can be converted to non-**IgE** binding sites by masking the site with a compd. that prevents **IgE** binding or by altering as little as a single amino acid within the **protein**, most typically a hydrophobic residue towards the center of the **IgE**-binding epitope, to eliminate **IgE** binding. The method allows the **protein** to be altered as minimally as possible, other than within the **IgE**-binding sites, while retaining the ability of the **protein** to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut allergens to demonstrate

alteration of **IgE** binding sites. The crit. amino acids within each of the **IgE** binding epitopes of the peanut **protein** that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of **IgE** binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to **IgE** binding.

L24 ANSWER 10 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 4
1999237932 EMBASE Mutant derivatives of the main respiratory allergen of cow are less allergenic than the intact molecule. Kauppinen J.; Zeiler T.; Rautiainen J.; Rytkonen-Nissinen M.; Taivainen A.; Mantyjarvi R.; Virtanen T.. T. Virtanen, Department of Clinical Microbiology, University of Kuopio, POB 1627, FIN-70211 Kuopio, Finland. Clinical and Experimental Allergy 29/7 (989-996) 1999.
Refs: 35.
ISSN: 0954-7894. CODEN: CLEAEN. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Background Allergen immunotherapy offers an alternative for drug treatment in the management of allergic diseases. Because immunotherapy often induces side-effects, less allergenic preparations would be beneficial. Objective The purpose of this study was to examine whether the allergenicity of a cow-derived lipocalin allergen, Bos d 2, could be diminished by substituting or deleting carboxy-terminal amino acids including the cysteine which forms a disulphide bond with a cysteine inside the molecule. Methods Four recombinant mutants of Bos d 2 were created by substituting or deleting the four most carboxy-terminal amino acids. The immunological characteristics of the mutant preparations were compared with the unmodified rBos d 2 by Western blotting, ELISA inhibition, skin prick tests, and the proliferative responses of allergen-specific T-cell clones. Results In Western blot, one of the two monoclonal antibodies showed reduced binding to the preparations without the terminal cysteine. In contrast, the other monoclonal antibody, human **IgE** and rabbit immune serum bound equally well to all the preparations. ELISA inhibition analyses revealed, however, that the preparations without the terminal cysteine bound antibody less efficiently. They were needed 15- 38 times more than the unmodified rBos d 2 to cause the same level of inhibition. Surprisingly, one of the mutants with the terminal cysteine but a mutated adjacent amino acid turned out to be the weakest in inducing skin reactivity. All the preparations stimulated well allergen-specific T-cell clones. Conclusions The results show that the allergenicity of a lipocalin allergen, Bos d 2, can be diminished by modifying the carboxy-terminal end of the molecule. Modifications in the area which encompasses a disulphide bond impaired the antibody binding without affecting the T-cell stimulatory capacity. It was also shown that in vivo tests are necessary for determining the allergenicity of a **modified allergen**.

L24 ANSWER 11 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 5
1999229161 EMBASE Genetically engineered plant allergens with reduced anaphylactic activity. Singh M.B.; De Weerd N.; Bhalla P.L.. Dr. M.B. Singh, Institute of Land and Food Resources, University of Melbourne, Parkville, Vic. 3052, Australia. International Archives of Allergy and Immunology 119/2 (75-85) 1999.
Refs: 81.
ISSN: 1018-2438. CODEN: IAAIEG. Pub. Country: Switzerland. Language: English. Summary Language: English.

AB Allergy immunotherapy is based on the administration of increasing amounts of the disease-eliciting allergens in order to yield allergen-specific non-responsiveness. Success of this therapy is associated with modulation of the immune response to allergenic molecules at the level of T-helper cells and the induction of blocking antibodies. The extracts used for immunotherapy are highly heterogenous preparations from natural sources

and contain additional components, mostly **proteins** which are not well defined. Recombinant DNA technology offers novel tools for production of pure and well-characterised allergens for specific immunotherapy. However, high **IgE** reactivity of pure recombinant allergens is associated with an increased risk of potentially life-threatening anaphylactic reactions. A major improvement in allergen-specific immunotherapy may be achieved by using genetically engineered recombinant allergens with reduced anaphylactic activity. Recently the site-directed mutagenesis technique has been applied successfully to produce variants of major grass, birch and oilseed rape allergens with reduced **IgE** reactivity but retained T-cell reactivity. These **modified allergens** with reduced anaphylactic potential are novel candidates for safer and more effective allergen-specific immunetherapy.

L24 ANSWER 12 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
1998417846 EMBASE Responses of human birch pollen allergen-reactive T cells to chemically **modified allergens** (allergoids). Dormann D.; Ebner C.; Jarman E.R.; Montermann E.; Kraft D.; Reske-Kunz A.B.. Dr. A.B. Reske-Kunz, Klinische Forschergruppe Allergie, Univ.-Hautklinik/Verfugungsgebaude, Obere Zahlbacher Strasse 63, D-55131 Mainz, Germany. Clinical and Experimental Allergy 28/11 (1374-1383) 1998. Refs: 29.
ISSN: 0954-7894. CODEN: CLEAEN. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB Background: Allergoids are widely used in specific immunotherapy for the treatment of **IgE**-mediated allergic diseases. Objective: The aim of this study was to analyse whether a modification of birch pollen allergens with formaldehyde affects the availability of T-cell epitopes. Methods: Efficient modification of the allergens was verified by determining **IgE** and IgG binding activity using ELISA inhibition tests. T-cell responses to birch pollen allergoids were analysed in polyclonal systems, using peripheral blood mononuclear cells (PBMC) of five birch pollen-allergic individuals, as well as birch pollen extract-reactive T-cell lines (TCL), established from the peripheral blood of 14 birch pollen-allergic donors. To determine whether the modification of natural (n)Bet v 1 with formaldehyde or maleic anhydride results in epitope-specific changes in T-cell reactivities, 22 Bet v 1- specific T-cell clones (TCC), established from nine additional birch pollen-allergic individuals, were tested for their reactivity with these products. Results: The majority of PBMC and TCL showed a reduced response to the birch pollen extract allergoid. Bet v 1-specific TCC could be divided into allergoid-reactive and -non-reactive TCC. No simple correlation between possible modification sites of formaldehyde in the respective T-cell epitopes and the stimulatory potential of the allergoid was observed. Mechanisms of suppression or of anergy reduction were excluded as an explanation for the non-reactivity of representative TCC. All TCC could be stimulated by maleylated and unmodified nBet v 1 to a similar extent. Conclusion: These results demonstrate differences in the availability of T-cell epitopes between allergoids and unmodified allergens, which are most likely due to structural changes within the allergen molecule.

L24 ANSWER 13 OF 23 SCISEARCH COPYRIGHT 2002 ISI (R)
97:381865 The Genuine Article (R) Number: WX987. Anti-IL-4 monoclonal antibody prevents antibiotics-induced active fatal anaphylaxis. Park J S; Choi I H; Lee D G; Han S S; Ha T Y; Lee J H; Lee W H; Park Y M; Lee H K (Reprint). CHONBUK NATL UNIV, SCH MED, DEPT IMMUNOL, CHONJU 561182, SOUTH KOREA (Reprint); CHONBUK NATL UNIV, SCH MED, DEPT IMMUNOL, CHONJU 561182, SOUTH KOREA; CHONBUK NATL UNIV, SCH MED, DEPT PATHOL, CHONJU 561182, SOUTH KOREA; CHONBUK NATL UNIV, SCH MED, INST MED SCI, CHONJU 561182, SOUTH KOREA; KOREAN RES INST CHEM TECHNOL, TAEJON, SOUTH KOREA; PUSAN NATL UNIV, SCH MED, DEPT MICROBIOL, PUSAN 609735, SOUTH KOREA. JOURNAL OF IMMUNOLOGY (15 MAY 1997) Vol. 158, No. 10, pp. 5002-5006. Publisher: AMER ASSOC

IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: SOUTH KOREA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We previously reported that anti-IL-4 mAb (11B11) failed to prevent **protein**-induced fatal murine anaphylaxis. To investigate the effect of anti-IL-4 on hapten-induced anaphylaxis, a model of murine anaphylaxis induced by antibiotics, penicillin V (Pen V) and cephalothin (CET), was developed, and the effect of anti-IL-4 on the anaphylaxis was observed. Pen V and CET induced 100 and 70 to 90% fatal reactions, respectively, when C57BL/6 mice were sensitized i.p. with 500 mu g of antibiotic-OVA conjugate with 2 x 10(9) Bordetella pertussis and 1.0 mg of alum and challenged i.v. with 100 mu g of antibiotic-BSA conjugate 14 days later. Serum taken from mice sensitized to Pen V passively sensitized normal mice to develop systemic anaphylaxis, and this ability of the serum was abrogated by heating at 56 degrees C for 2 h or depletion of **IgE**, but not IgG, Abs. Thus, the antibiotic-induced fatal reaction was an **IgE**-dependent anaphylactic reaction. Administration of anti-IL-4 at the beginning of sensitization completely prevented the fatal anaphylactic reactions to both Pen V and CET. This effect of anti-IL-4 was associated with its suppressive activity on antibiotic-specific serum **IgE**, but not IgG, levels. More importantly, anti-IL-4 therapy in previously sensitized mice was also effective in preventing the fatal reactions and rapidly reduced the established **IgE** levels. This study provides a new animal model of hapten-induced anaphylaxis and indicates that blocking of IL-4 activity may be beneficial in allergic diseases caused by a variety of haptens in which **IgE** Abs play a major role.

L24 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2002 ACS
1995:680795 Document No. 123:81614 Recombinant preparation of **modified allergen** Der fII as antiallergic agents.
Nishama, Chiharu; Juki, Toshifumi; Okumura, Yasushi; Shibuya, Ichiro (Asahi Breweries Ltd, Japan; Torii Yakuhin Kk; Nikka Whisky). Jpn. Kokai Tokkyo Koho JP 07095887 A2 19950411 Heisei, 50 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1993-275897 19930929.

AB Allergen Der fII of Dermatophagoides farinae is modified by replacing certain residues with Ala to lower its **IgE**-binding activities. The **modified allergen** can be produced by expressing its coding gene in an eukaryotic host and used as an antiallergic agent.

L24 ANSWER 15 OF 23 SCISEARCH COPYRIGHT 2002 ISI (R)
95:275917 The Genuine Article (R) Number: QT138. ALLERGENS FROM HOUSE-DUST MITES OF THE GENUS DERMATOPHAGOIDES - NATURE, ANTIGENIC AND STRUCTURAL CHARACTERIZATION, AND MEDICAL PREPARATIONS. KHLGATYAN S V (Reprint); PEROVA N A. RUSSIAN ACAD MED SCI, MECHNIKOV INST VACCINES & SERA, PER MECHNIKOVA 5A, MOSCOW 103064, RUSSIA (Reprint). BIOCHEMISTRY-MOSCOW (FEB 1995) Vol. 60, No. 2, pp. 155-167. ISSN: 0006-2979. Pub. country: RUSSIA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Microscopic mites of the genus Dermatophagoides are the major source of house dust allergens. Four homologous classes of main allergens have been isolated from extracts prepared from the mites D. pteronyssinus and D. farinae. The main mite allergens are generally believed to be **proteins** of gastrointestinal origin. Group I mite allergens Der pI and Der fI are thermolabile glycoproteins with molecular weight 25 kD. Comparison of primary structures revealed 30% homology between group I mite allergens and cathepsins B and H, papain, and actinidin. The allergens are proteolytic enzymes (cysteine proteinases). Study of allergenic composition revealed three common and two species-specific epitopes on Der pi and Der fI. The amino acid sequences of major allergenic determinants of Der pI were established. Group II mite allergens Der pII and Der fII are single-chain thermally stable **proteins** with molecular weights of 10-14 kD. Group II allergens

are believed to be analogous to trypsin. Der pIII and Der fIII showed 50% homology in amino acid sequences with serine proteinases found in vertebrates and invertebrates. Mite amylase (56-60 kD) is a member of the fourth group of main mite allergens. There is considerable homology between group IV allergens and mammalian alpha-amylase. All mite allergens induce production of specific **IgE** antibodies in humans. The use of purified allergens improves the quality of diagnosis and treatment of mite allergoses. Modified forms of mite allergens (allergoids, carrier-adsorbed allergens, and liposome-bound preparations) are now successfully used in specific immunotherapy.

L24 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2002 ACS
1995:993912 Document No. 124:84231 Influence of formaldehyde modification on the physico-chemical properties and specific activity of Dermatophagoides farinae mite allergens. Perova, N. A.; Emelyanova, O. Yu.; Khlgatian, S. V.; Berzhets, V. M. (Mechnikov Res. Inst. of Vaccines and Sera, Moscow, Russia). Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii (2), 92-5 (Russian) 1995. CODEN: ZMEIAV. ISSN: 0372-9311. Publisher: Meditsina.
AB D. farinae allergen has been modified with formaldehyde and its properties were studied. This study has demonstrated that the formolation of D. farinae mite allergen causes changes in isoelec. points of **proteins** and a shift of the **protein** fraction to acidic pH values: 3.0-4.85; an insignificant decrease in the vol. of gel filtration output on a column packed with Sephacryl S-300; and a decrease in the esterase activity from 10.5 to 1.8 .mu.M tosylarginine Me ester/min/mg of **protein**. As revealed with the use of microdot enzyme immunoassay, the **modified allergen** loses its capacity to bind to human specific **IgE** antibodies in vitro.

L24 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2002 ACS
1993:232264 Document No. 118:232264 Ryegrass pollen allergen. Singh, Mohan Bir; Hough, Terryn; Knox, Robert Bruce; Theerakulpisut, Piyada; Smith, Penelope; Avjioglu, Asil; Ong, Eng Kok (University of Melbourne, Australia). PCT Int. Appl. WO 9304174 A1 19930304, 121 pp. DESIGNATED STATES: W: AU, CA, DK, JP, KR; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-AU430 19920814. PRIORITY: US 1991-746702 19910816.
AB Nucleic acid sequences are disclosed which code for 2 ryegrass pollen allergen Lol p Ib family members, as are purified Lol p Ib.1 and Lol p Ib.2 **proteins** and fragments thereof, methods for producing the recombinant Lol p Ib.1 and Lol p Ib.2 or fragments, derivs., or homologs thereof, and methods of using the nucleic acids and **proteins**. Cloning of allergen genes is described, and nucleotide sequences (and corresponding amino acid sequences) for nucleic acids coding Lol p Ib.1 and Lol p Ib.2 are included. Allergen epitopes were delineated with **IgE** and monoclonal antibodies (MAbs). Prodn. of MAbs against Lol p Ib.1 is also described. RNA was extd. from Lolium perenne flowerheads, and PCR was used in anal. of polymorphism of the genes encoding Lol p Ib.1 and Lol p Ib.2.

L24 ANSWER 18 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 6
90206447 EMBASE Document No.: 1990206447. Allergen-directed expression of Fc receptors for **IgE** (CD23) on human T lymphocytes is modulated by interleukin 4 and interferon-.gamma.. Prinz J.C.; Baur X.; Mazur G.; Rieber E.P.. Institute for Immunology, Ludwig-Maximilians-University, Goethestr. 31,D-8000 Munich 2, Germany. European Journal of Immunology 20/6 (1259-1264) 1990.
ISSN: 0014-2980. CODEN: EJIMAF. Pub. Country: Germany. Language: English. Summary Language: English.
AB T lymphocytes bearing Fc receptors (FcR) for immunoglobulins are known to have immunoglobulin class-specific regulatory functions. Here we report that expression on T cells of the low-affinity FcR for **IgE** (Fc.epsilon.RII/CD23) is preferentially induced by stimulation with

antigens that cause an **IgE** response. T cells from eight patients allergic to the hemoglobin of Chironomus thummi thummi mosquito larvae (CHIT I) were analyzed for reactivity with the anti-FcERII/CD23 monoclonal antibody (mAb) M-L25 under various conditions. No Fc.epsilon.RII/CD23+ T cells were observed among freshly isolated, resting peripheral blood mononuclear cells (PBMC). Stimulation of PBMC with CHIT I, however, induced a marked although transient Fc.epsilon.RII/CD23 expression on a large portion of the allergen-activated T lymphocytes. It reached a maximum of 37.2 .+-. 4.6% Fc.epsilon.RII/CD23+ T cell blasts on day 5 of culture. The selectivity of this expression became evident when compared to non-allergenic control antigens: after stimulation of PBMC with tetanus toxoid or purified **protein** derivative from tuberculin a maximum of 4.6% .+-. 1.4% and 4.2% .+-. 1.1% T cell blasts was found to express Fc.epsilon.RII/CD23, respectively. Activation by an anti-CD3 mAb was insufficient to induce Fc.epsilon.RII/CD23 on T cells. The allergen-stimulated Fc.epsilon.RII/CD23+ T cells exclusively belonged to the CD4+CD29+ helper inducer T cell subset. Using a cDNA probe coding for the B cell Fc.epsilon.RII/CD23, Northern blot analysis revealed a 1.7-kb Fc.epsilon.RII/CD23 mRNA in extracts of highly purified allergen-stimulated T cells. It was of the same size as Fc.epsilon.RII/CD23 of the lymphoblastoid B cell line WI-L2. Of several cytokines tested [interleukin (IL) 1 to IL 6, interferon-.gamma. (IFN-.gamma.), tumor necrosis factor-.alpha.] only IL 4 and IFN-.gamma. significantly **modified allergen**-induced Fc.epsilon.RII/CD23 expression on T cells. The latter was enhanced nearly twofold in the presence of IL 4, and was almost completely abrogated by IFN-.gamma.. IL 4, however, could not increase the number of Fc.epsilon.RII/CD23+ T lymphocytes either alone or in combination with an anti-CD3 mAb. Taken together, the selective induction of Fc.epsilon.RII/CD23 on T cells by allergen and its inclusion in the regulatory network of cytokines point to an important role of Fc.epsilon.RII/CD23+ T lymphocytes in the human **IgE** response.

L24 ANSWER 19 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 7

83120295 EMBASE Document No.: 1983120295. Antigen- and **IgE** class-specific suppression mediated by T suppressor cells of mice treated with glutaraldehyde-polymerized ovalbumin. HayGlass K.T.; Strejan G.H.. Dep. Microbiol. Immunol., Univ. West. Ontario, London, Ont. N6A 5C1, Canada. International Archives of Allergy and Applied Immunology 71/1 (23-31) 1983.

CODEN: IAAAAM. Pub. Country: Switzerland. Language: English.

AB Various size polymers are obtained following glutaraldehyde treatment of native ovalbumin (OA). OA-POL, approximately 35x106 daltons, was prepared at the isoelectric point of OA. Treatment of CBA mice with microgram amounts of OA-POL led to efficient antigen-specific suppression of **IgE** responses. IgG anti-OA antibodies were not suppressed. Transfer of cells from OA-POL-treated donors into normal, unprimed recipients interfered with the ability of these animals to mount a primary or secondary **IgE** response. In addition, cotransfer of spleen cells from OA-POL-treated mice along with OA (in alum)-primed cells, into irradiated syngeneic recipients resulted in **IgE** class-specific suppression that was abrogated by treatment of OA-POL donor cells with monoclonal anti-Thy 1.2 + complement. The presence or absence of T cells in the OA-POL population had no effect on IgG levels in the recipients. Analysis of the antigen properties of OA-POL revealed 5-15% cross-reactivity with native OA as perceived by IgG or **IgE** antibodies. In contrast, OA-POL was highly cross-reactive at the T cell level as shown functionally by its potent induction of OA-specific, **IgE**-selective suppressor T cells. The results suggest that the beneficial effects of glutaraldehyde-**modified allergens**, recently introduced in the immunotherapy of atopic individuals may be due to the preferential exposure on the polymerized **protein**, of antigenic determinants generating T suppressor cells and to the selective

loss of B cell-reactive determinants.

L24 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2002 ACS
1981:63620 Document No. 94:63620 Suppression of reaginic antibodies with **modified allergens**. IV. Induction of suppressor T cells by conjugates of polyethylene glycol (PEG) and monomethoxy PEG with ovalbumin. Lee, W. Y.; Sehon, A. H. (Fac. Med., Univ. Manitoba, Winnipeg, MB, Can.). Int. Arch. Allergy Appl. Immunol., 64(1), 100-14 (English) 1981. CODEN: IAAAAM. ISSN: 0020-5915.

AB Administration of multiple injections of conjugates of ovalbumin (OA) and PEG or its monomethoxy deriv. (mPEG) into mice which were sensitized with 2,4-dinitrophenylated OA (DNP3-OA) abrogated both the anti-OA and anti-DNP **IgE** responses, in spite of addnl. injections of the sensitizing dose of DNP3-OA in the presence of Al(OH)3. Treatment of mice with OA-PEG in Al(OH)3 stimulated preferentially helper T cells, whereas injection of mice with OA-PEG in the absence of adjuvant elicited predominantly suppressor T cells. The unresponsive state of mice which were treated 21 days earlier with OA-PEG could not be broken by the transfer of normal spleen cells and an addnl. sensitizing dose of DNP3-OA. Transfer of spleen cells from tolerized animals to normal mice dampened the capacity of the latter to mount both anti-DNP and anti-OA **IgE** reponses; however, the suppressive effect of these cells was eliminated by treatment of the normal recipients with cyclophosphamide, a procedure known to inactivate suppressor T cells; probably, this effect was not due to the carryover of the tolerogen with the transferred cells. Apparently, the suppressor cells induced by the treatment of mice with OA-PEG and OA-mPEG conjugates belongs to a T cell subpopulation, and the B cells of these mice were devoid of suppressive activity.

L24 ANSWER 21 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 8
81023748 EMBASE Document No.: 1981023748. Suppression of reaginic antibodies with **modified allergens**. III. Preparation of tolerogenic conjugates of common allergens with monomethoxypolyethylene glycols of different molecular weights by the mixed anhydride method. Wie S.I.; Wie C.W.; Lee W.Y.; et al.. Dept. Immunol., Univ. Manitoba Bas. Med. Sci. Bldg., Winnipeg, Manitoba R3E 0W3, Canada. International Archives of Allergy and Applied Immunology 64/1 (84-99) 1981.
CODEN: IAAAAM. Pub. Country: Switzerland. Language: English.

AB Our previous findings that antigens, such as ovalbumin (OA) and the extract of ragweed pollen (RAG), could be rendered nonantigenic, nonallergenic and tolerogenic by conjugation with polyethylene glycol (PEG) have been extended in the present to the synthesis of conjugates of a variety of antigens with monofunctional monomethoxy-PEGs (mPEGs) of different molecular weights by the use of the mixed anhydride method. Thus, mPEGs with molecular weights of 2,000, 5,000, 10,000 and 20,000 were coupled to **proteins** such as dog serum albumin (DA), bovine pancreatic ribonuclease, OA and the constituents of pollen, helminth and bacterial allergens (RAG, Timothy grass pollen, Ascaris suum and Micropolyspora faeni). All these mPEG conjugates depressed markedly the ongoing **IgE** antibody formation in sensitized animals, in spite of additional injections of the sensitizing dose of the appropriate antigen. Moreover, the allergenicity of the **proteins** was either totally abolished or markedly reduced after coupling to mPEGs. Conjugates of DA and OA of varying degree of substitution (i.e. number of mPEG molecules attached per **protein** molecule) were prepared with mPEGs of different molecular weights and their immunological properties were assessed. It appears that, for a series of tolerogenic conjugates of the same antigen, there exists some inverse relationship between the degree of substitution and the molecular weight of mPEG, i.e. a high level of tolerogenicity with a concomitant reduction or total loss of allergenicity was achieved with a lower degree of substitution utilizing mPEGs of increasing molecular weights. On the basis of these results, it is concluded that a variety of allergens may be converted by conjugation

with mPEGs to tolerogenic products with a potential for use in the therapy of patients allergic to a wide spectrum of common allergens.

L24 ANSWER 22 OF 23 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 9

1978:171952 Document No.: BA65:58952. SUPPRESSION OF REAGINIC ANTIBODIES WITH **MODIFIED ALLERGENS** PART 1 REDUCTION IN ALLERGENICITY OF **PROTEIN** ALLERGENS BY CONJUGATION TO POLY ETHYLENE GLYCOL. LEE W Y; SEHON A H. DEP. IMMUNOL., FAC. MED., UNIV. MANIT., WINNIPEG, MANIT. R3E 0W3, CAN.. INT ARCH ALLERGY APPL IMMUNOL, (1978) 56 (2), 159-170. CODEN: IAAAAM. ISSN: 0020-5915. Language: English.

AB The conjugates of ovalbumin (OA) and of the nondialyzable constituents of the aqueous extract of ragweed pollen (RAG) with polyethylene glycols of MW of 6000 or 20,000 (PEG6 or PEG20) were nonantigenic, nonallergenic and nonimmunogenic. The i.v. administration of OA-PEG and RAG-PEG conjugates into mice did not elicit antibodies to OA and RAG, respectively, and these conjugates suppressed in an immunologically specific manner the capacity of these animals to mount primary as well as secondary Ig[immunoglobulin]E responses to sensitizing doses of dinitrophenylated OA or of RAG. The PEG-modified antigens did not combine in vitro or in vivo with **IgE** antibodies directed against the natural antigens. OA-PEG and RAG-PEG conjugates were incapable of triggering allergic reactions in animals possessing **IgE** antibodies to the unmodified antigens. These PEG-modified antigens were tolerogenic.

L24 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2002 ACS

1977:550075 Document No. 87:150075 Abrogation of reaginic antibodies with **modified allergens**. Lee, Weng Y.; Sehon, Alec H. (Fac. Med., Univ. Manitoba, Winnipeg, Manitoba, Can.). Nature (London), 267(5612), 618-19 (English) 1977. CODEN: NATUAS.

AB The **protein** antigen, ovalbumin, and the mixt. of nondialyzable allergenic constituents of the aq. ext. of ragweed pollen were coupled to polyethylene glycol, thereby converting them to tolerogenic and nonallergenic products which were capable of abrogating the primary as well as ongoing **IgE** responses to the corresponding native allergens in B6D2F1 mice and rats. These allergen conjugates did not react with antibodies to the unmodified allergens and did not induce any antibody response; they may therefore prove to be useful therapeutic agents for the abrogation of **IgE**-mediated allergies without unleashing anaphylactic reactions. The suppressive effects of the modified antigens may be mediated by suppressor cells specific for the determinants of the carrier portion of the native antigen.

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CA SUBSCRIBER PRICE	-9.29	-9.29

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L9 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:321272 HCAPLUS
DOCUMENT NUMBER: 120:321272
TITLE: Recognition of **T cell** epitopes and lymphokine secretion by rye grass **allergen** Lolium perenne I-specific human **T cell** clones
AUTHOR(S): Spiegelberg, Hans L.; Beck, Lucinda; Stevenson, Donald D.; Ishioka, Glenn Y.
CORPORATE SOURCE: Dep. Pediatr., Univ. California, San Diego, La Jolla, CA, 92093, USA
SOURCE: J. Immunol. (**1994**), 152(9), 4706-11
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 15-9 (Immunochemistry)
ABSTRACT:

T cell lines (TCL) and CD4+ **T cell** clones (TCC) with specificity for the rye grass **allergen** Lolium perenne (Lol p) I were isolated from the blood of nine donors, six having active atopic disease, two being in remission, and one having **IgE** anti-Lol p I Abs but not atopic disease. The **T cell** epitopes of Lol p I were detd. by TCLs and TCCs reactivity with 23 overlapping, 20 **amino acid**-long peptides spanning the entire length of the 230 **amino acid**-long **allergen**. In addn., the Th subsets (Th1, Th2, Th0, Thp) were detd. by measuring IL-2, IFN-.gamma., and IL-4 in the supernatants of TCC **activated** with Lol p I and irradiated APC. TCC from individuals from which a large panel of clones were obtained from 105 PBMC initial cultures recognized multiple peptides (5-9) and of 23 overlapping peptides a total of 16 were recognized by at least one TCC from one of the patients. These 16 peptides were derived from all areas of the Lol p I mol., indicating the ability of human Th cells to recognize many peptide epitopes on Lol p I. Although no clear cut immunodominant peptides were detected, **T cell** clones of 50% of the patients reacted with peptide 191-210. There was no correlation between peptide epitope reactivity and lymphokine secretion pattern of the TCC. Of 12 TCC obtained from six patients with active atopic disease, four (33%) were of Th1, five (42%) of Th2, one (8%) of Thp, and two (17%) of Th0 type. Of 14 TCCs isolated from three atopic donors in remission, five (36%) were of Th1, three (21%) of Th2, four (29%) of Thp, and two (14%) of Th0 type. The data demonstrate that T ***cells*** from rye grass pollen allergic patients can recognize multiple peptide epitopes on Lol p I scattered over the entire mol. No correlation existed between epitope reactivity and lymphokine secretion pattern of the TCC.

SUPPL. TERM: helper lymphocyte epitope rye grass **allergen**; Lolium **allergen** epitope **T cell**
INDEX TERM: Lolium
(**allergen** I of pollen of, human helper **T-cell** epitopes of)
INDEX TERM: Molecular structure-biological activity relationship
(helper **T-cell**-stimulating, of **allergen** I of rye grass pollen)
INDEX TERM: **Allergens**

ROLE: BIOL (Biological study)
(Lol p I (Lolium perenne, I), helper **T-cell** subsets to, epitopes for human)

INDEX TERM: Lymphocyte
(**T-cell**, helper cell, to **allergen** I of rye grass, epitope for human precursor)

INDEX TERM: Lymphocyte
(**T-cell**, helper cell/inducer, Th2, to **allergen** I of rye grass, epitope for human)

INDEX TERM: Lymphocyte
(**T-cell**, helper cell/inducer, TH0, to **allergen** I of rye grass, epitope for human)

INDEX TERM: Lymphocyte
(**T-cell**, helper cell/inducer, TH1, to **allergen** I of rye grass, epitope for human)

INDEX TERM: Allergy
(atopic, for rye grass pollen, helper **T-cell** epitopes on Lol p I **allergen** of humans with)